REMARKS

I. Status of the claims

Claims 44-74 are pending. Claims 57-69 and 71-74 remain withdrawn and claims 1-41 remain cancelled. No claims have been amended in this response.

II. Rejections under 35 U.S.C. § 112, first paragraph

The examiner has rejected claims 44-56, and 70 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The examiner agrees that motifs with respect to the GC base pairs, positions, and overhangs have been adequately described, but that adequate description for siRNAs that are not fully complementary to target sequence and which antisense and sense strands are not complementary with respect to each other are not adequately described. One skilled in the art, according to the examiner, would therefore reasonably conclude that adequate written description is lacking for the genus of inhibitory compounds claimed by Applicants.

Applicants respectfully disagree. While the examiner has concluded that the specification does not adequately disclose double stranded RNA (dsRNA) where the sense and antisense strands are not fully complementary to each other and antisense strand is not fully complementary to target sequence, this does not take into account a complete analysis of the specification. According to MPEP §2163, if a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g., *Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in *ipsis verbis* [i.e., "in the same words"] to be sufficient").

Applicants direct the examiner's attention to paragraphs [0026], [0027], [0033] and [0048] of the published application. These paragraphs describe dsRNAs wherein the two strands are not fully complementary to each other and where the antisense strand is not fully complementary to the target sequence. For instance, paragraph [0026] describes "dsRNA" as referring to a ribonucleic acid having a duplex structure comprising two complementary and anti-parallel nucleic acid strands and "dsRNA" that includes short interfering RNA (siRNA);

paragraph [0026] also discloses that "[n]ot all nucleotides of a dsRNA must exhibit Watson-Crick base pairs; the two strands may be substantially complementary"; paragraph [0027] states that "sense strand need only be substantially complementary with the antisense strand to maintain the overall double-stranded character of the molecule"; and paragraph [0033] discloses that the term "double-stranded" means "two separate strands comprising a region in which at least a portion of the strands are sufficiently complementary to hydrogen bond and form a duplex structure."

Paragraph [0027] further discloses that dsRNA includes a region which is "at least partially complementary to the target." Thus, it is "not necessary that there be perfect complementarity between the dsRNA and the target"; complementarity need only be sufficient to enable the dsRNA to direct sequence specific RNAi cleavage of the target. See paragraph [0027]. In describing specific embodiments, paragraph [0027] also states that the antisense strand can comprise one or more but preferably 6, 5, 4, 3, 2, or fewer mismatches with respect to the target RNA. Additionally, dsRNA having at least 70%, 85%, 90% or 95% sequence identity between the sense strand and the target RNA are encompassed by the invention. See paragraph [0048].

Thus, paragraphs [0026], [0027], [0033] and [0048] describe how the claimed dsRNAs include various siRNAs, not just those that are fully complementary with respect to each strand and not just those in which the antisense strand is fully complementary to the target sequence.

As noted in the previous response, example 5 demonstrates that specific placement of GC base pairs in the dsRNA results in dsRNA serum stability, and example 6 demonstrates that specific placement of GC base pairs results in increased thermodynamic stability of the dsRNA. Both of these examples show that the GC base pairs set forth in the manner recited in the Applicants' claimed invention lead to an improved capacity of the dsRNA to mediate RNA interference.

Taking into account the entire disclosure, one skilled in the art would be able to apply the disclosure of paragraphs [0026], [0027], [0033] and [0048] to examples 5 and 6 with an expectation that exemplified dsRNA could be extended to dsRNAs where the two strands are not fully complementary and the antisense strand is not fully complementary to the target. Therefore, based on the entire disclosure, it is clear that the inventors had adequately described

and had possession of the claimed invention, including dsRNAs where the sense and antisense strand were not fully complementary to each other and the antisense strand was not fully complementary to the target RNA.

Certainly, the examiner has not presented sufficient evidence or reasoning to rebut the presumption that written description, including the specification and the claims, is adequate. See *In re Wertheim*, 541 F.2d 257, 263 (CCPA 1976), (the examiner has the initial burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims).

Accordingly, Applicants respectfully request the examiner withdraw this rejection under 35 U.S.C. § 112, first paragraph.

III. Conclusion

Except for issue fees payable under 37 C.F.R. §1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 19-2380. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. §1.136(a)(3).

Respectfully submitted,

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